REMARKS

Claims 1-83 are pending. Claims 1, 5, 9-15, 32-33 and 83 are under examination. Claims 2-4, 6-8, 16-31 and 34-82 are withdrawn from consideration. Claims 14, 15, 33 and 83 are objected to for being in improper form under Rule 1.75(c). Claims 1, 5, 9-15, 32-33 and 83 are objected to because claims 1, 5, 9-15 recite nonelected subject matter in the alternative. Claims 32-33 and 83 are objected to for depending on the claims under objection. The Examiner also alleges that claims 9-12 are considered identical in scope and therefore, improper as being duplicative. Claims 1, 5, 9-13 and 32 are rejected under 35 U.S.C. § 112, first paragraph for allegedly not being enabled by the specification. Claims 1, 13 and 32 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly not satisfying the written description requirement.

This Response addresses each of the Examiner's rejections. Applicants therefore respectfully submit that the present application is in condition for allowance. Favorable consideration of all pending claims is therefore respectfully requested.

Amendments to Claims

Claims 1, 5, 13, 16, 32-33 and 83 have been amended in accordance with the foregoing claim listing. Claims 9-12 and 14-15 are cancelled.

Claim 1 has been amended to specify determining colorectal adenoma in a human employing a nucleic acid molecule comprising SEQ ID NO: 7 or a sequence that hybridizes to the complement of SEQ ID NO: 7. Support for this amendment is found on page 23, line 11, and page 29, line 8 of the specification, and original claim 15.

Claim 16 has been amended to specify the determination of the colorectal adenoma of a human. Support is found for amended claim 16 on, for example, page 23, line 11, and page 29,

line 8 of the specification, and original claims 1 and 15. Claims 32-33 have been amended to specify human colorectal adenoma or biopsy tissue. Support for the amendments to claims 32-33 is found on page 23, lines 3-6 of the specification, for example.

Applicants respectfully submit that the foregoing amendments do not introduce new matter.

Objections to the Claims

The Examiner has objected to claims 13, 14, 33 and 83 as being of improper form in that they are multiple dependent claims that depend from a multiple dependent claim.

Applicants respectfully submit that claim 14 has been canceled, rendering the objection thereof moot. Claims 13, 33 and 83, as amended, are not improper.

Claim 15 has been objected to because it depends on claim 14. The objection is moot in view of the cancellation of the claim.

Claims 1, 5, 9-15, 32-33 and 83 are objected to because claims 1, 5 and 9-15 recite non-elected subject matter in the alternative. It is respectfully submitted that the claims, as amended, properly reflect the elected subject matter (SEQ ID NO: 7).

The Examiner also alleges that claims 9-12 are considered identical in scope. It is respectfully submitted that claims 9-12 have been canceled without prejudice.

Accordingly, the objections to the claims are overcome and withdrawal thereof is respectfully requested.

Rejection Under 35 U.S.C. § 112, first paragraph – Enablement Requirement

Claims 1, 5, 9-13 and 32 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly not being enabled by the specification.

The Examiner contends that claims 1, 5, 9-13 and 32 encompass a method of determining the onset or predisposition to the onset of a gastrointestinal tract neoplasm in an individual by measuring the level of expression of a nucleic acid comprising SEQ ID NO:7 or a nucleic acid that hybridizes to SEQ ID NO: 7 at high stringency in a biological sample. The Examiner has alleged that the claimed methods are not enabled with respect to any "individual", or any "gastrointestinal tract neoplasm", or with respect to determination of the predisposition to the onset of a gastrointestinal tract neoplasm.

To expedite the allowance of the pending claims, Applicants have amended the claims by deleting references to "individual" and replacing with the term "human." Similarly, the term "gastrointestinal tract neoplasm" has been deleted, and the claims presently recite "colorectal adenoma." The expression of "the predisposition to the onset of" has also been deleted from the claims. Applicants reserve the right to file continuation applications in relation to the subject matter presented in the claims as originally filed.

The Examiner alleges that the field of gene expression is unpredictable and therefore concludes that it would require undue experimentation for the person of ordinary skill in the art to practice the full scope of the claimed method. The Examiner cites *Mycogen Plant Sci. v. Monsanto Co.*, 243 F.3d 1316, 1330 (Fed. Cir. 2001) in support of her position.

Applicants respectfully disagree with the Examiner's application of the unpredictability doctrine per *Mycogen* to the subject matter of the pending claims. In *Mycogen*,

the court stated, "[t]he examiner observed that the disclosure was enabling only for the specific sequence shown in Figure 1, and that in view of the unpredictability of ***foreign gene expression***, it did not appear that any functionally equivalent synthetic gene would be effective in any plant cell." (Emphasis added). Applicants respectfully submit that the claimed subject matter has nothing to do with gene transfer in heterologous system. Instead, the claimed method is directed to a diagnostic screen which is based on screening for the expression level of one or more specific nucleic acid molecules, one of which comprises SEQ ID NO: 7 or a sequence that hybridizes to the complement of SEQ ID NO: 7.

Therefore, the unpredictability issue raised by the Examiner is not applicable to the presently disclosed and claimed subject matter. Put another way, the claimed method of measuring gene expression is not unpredictable, since there is no unpredictability regarding whether or not the method will yield a result, i.e., measurement of the expression level of relevant nucleic acid molecules. Therefore, in the absence of the technical issues that may be associated with the expression of foreign genes, it is respectfully submitted that the Examiner's rationale does not establish a *prima facie* case of non-enablement of the claimed subject matter on this basis alone.

In addition, the Examiner contends that the claims are not enabled with respect to any "biological sample". The Examiner contends that even if the claims were limited to screening for colorectal biopsies in a human, there is no guidance in the specification that teaches one how to practice the invention. Specifically, the Examiner alleges that there is no demonstration in the specification of the range of values one would be looking for in terms of a percentage increase above normal.

The Examiner has misinterpreted the invention in that Applicants are not claiming a specific percentage above the normal but, rather, are claiming that any level of expression above the normal is indicative of adenoma development. The specification fully supports this finding. Applicants respectfully direct the Examiner's attention to lines 10-25 of page 29 in the specification, that describes, *inter alia*, the common use of relative analysis assays, and to Tables 3-4 (pages 115-116) showing markers with differing fold of up-regulation.

The Examiner alleges that the specification is silent with respect to the number of samples that were used to obtain the mean value for normal tissues. Applicants respectfully disagree and direct the Examiner's attention to page 100, lines 15-27, wherein the number of tissue samples and status as normal and adenoma are provided. Further, Applicants respectfully submit that it is routine for those skilled in the art to determine the "normal" control value as the basis for comparison.

The Examiner also alleges at page 8 of the Office Action that "there is no external working example which validates the use of SEQ ID NO: 7 as a marker for colorectal adenoma." The basis for the Examiner's allegation in this regard is unclear. The specification clearly shows that clones 8-2d and 12-2f, i.e., nucleic acid molecules to which SEQ ID NO: 7 corresponds, were up-regulated by 50 and 45 fold, respectively, in adenoma tissue samples. See page 100, line 15 to page 101, line 13, and Table 3 on page 115.

Further, Applicants respectfully submit that SEQ ID NO: 7 corresponds to KIAA1199, a molecule known to those skilled in the art, as evidenced by its sequence in Genbank under Accession No. NC-000015. Therefore, given SEQ ID NO: 7, those skilled in the art would readily identify, for example, by Blasting the Genbank database, the KIAA1199 gene.

Therefore, the Examiner's allegation that one would not know what gene SEQ ID NO: 7 corresponds is unfounded.

As far as performing a diagnostic assay, as opposed to performing the differential display analysis which appears in the specification, techniques for screening for changes in the level of expression of mRNA or a protein are well known and have been performed as a matter of routine procedure for over 20 years. It would be improper for the Examiner to take the position that performing these types of assays requires undue experimentation in a situation where Applicants have directed the skilled person to a particular molecule or molecules which must be analyzed (i.e., a nucleic acid comprising SEQ ID NO: 7 or a sequence that hybridizes to the complement of SEQ ID NO: 7), and where the techniques which are to be used are so routine.

In sum, it is respectfully submitted that the evidence and guidance provided by the specification, together with the knowledge of persons of ordinary skill in the art, clearly enable the claimed methods. This is especially clear when considering the scope of the claim amendments submitted herein, which are believed to directly address a number of the Examiner's key concerns.

Therefore, it is respectfully requested that the Examiner withdraw the rejection based on the alleged non-enabling disclosure provided in the specification.

Rejection Under 35 U.S.C. § 112, first paragraph – Written Description Requirement

Claims 1, 13 and 32 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly not satisfying the written description requirement.

Applicants respectfully submit that several of the issues raised by the Examiner have

been addressed by the foregoing amendments. For example, the claims have been amended by deleting references to methods of determining a predisposition toward developing a neoplasm, by specifying the "individual" as a human subject, and by reciting "colorectal adenoma" specifically. Further, Applicants respectfully submit that the present claims do not include any reference to "functional derivative, variant or homologue".

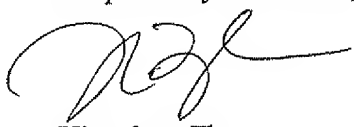
The Examiner also alleges that the genus of nucleotide sequences capable of hybridizing to any one or more of the sequences of SEQ ID NO: 7 under high stringency conditions is not adequately described in the specification.

In response, Applicants respectfully submit that nucleic acids claimed based on hybridization language may be considered to have met the written description requirement, because highly stringent hybridization conditions dictate that the species within the claimed genus are structurally similar, i.e., similar in sequence to the recited sequence in the claims. See, Enzo Biochem, In.c. v. Gen-Probe Inc., 323 F.3d 956, 967-968 (Fed. Cir. 2002).

Accordingly, it is respectfully requested that the rejection under 35 U.S.C. § 112, first paragraph be withdrawn.

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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